

Advanced Dementia Palliative Care Study Protocol

Administrative Information

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Protocol Introduction

Background

3.A.i Improving advanced dementia palliative care is a compelling public health priority. Alzheimer's disease and other dementias affect more than 5 million Americans and their family caregivers.¹ Societal costs were \$157-215 billion in 2010, largely due to Medicaid long-term care and family caregiving expenses.² Dementia is associated with increased rates of hospitalization, care transitions, and 30-day readmissions.³ Medications may slow progression, but current research offer little hope of cure.^{4,5} Patients live 3-9 years after diagnosis, and dementia is a contributing cause for 1 in 3 deaths.^{6,7,8} Dementia is the only leading cause of death in the U.S. with no meaningful preventive or curative intervention; as a result, prevalence is expected to double by 2030.⁹

Approximately 1 million Americans have advanced dementia, the final and most symptomatic stage of illness. Using the Global Deterioration Scale (GDS) staging system, advanced dementia is characterized by profound memory deficits, inability to recognize family members, sparse speech, incontinence, and dependence for all activities of daily living.¹⁰ The cohort of persons with advanced dementia enrolled in the Choices, Attitudes, and Strategies for Care of Advanced Dementia at the End-of-Life (CASCADE) Study had a 6-month mortality risk of 25% and median survival of 1.3 years.¹¹

3.A.ii Advanced dementia care places extraordinary demands on family caregivers. Dementia results in a prolonged course of functional dependency.¹² Family caregivers provide care an estimated 22 hours per week.¹³ Caregiving lasts an average of 3 years, with significant loss of paid work.¹⁴ A high portion of the cost of care is borne by family caregivers; out-of-pocket family expenses average \$66,000 in the last year of life – more than any other cause of death.¹⁵

3.A.iii Current advanced dementia care is poor quality -- high symptom distress, poor communication about goals of care, and limited hospice access. Current care for patients with advanced dementia rarely meets standards for high quality palliative care. Distressing symptoms such as pain, shortness of breath, neuropsychiatric symptoms, feeding problems, and problems with incontinence and personal cleanliness are common in advanced dementia, and severity worsens as death approaches.^{11,16,17, 18, 19, 20} Cognitive impairment is a risk factor for under-treatment of pain, and up to 50% of dementia patients experience frequent and unrelieved pain during their last year of life.^{21, 22,23}

Compared with advanced cancer patients, persons with advanced dementia are rarely recognized as terminally ill, and less likely to have decisions about life-sustaining treatment.^{24,25} Burdensome medical treatments are common. In CASCADE 40.7% of patients experienced at least one hospitalization, emergency transfer, parenteral therapy or tube feeding during the final 3 months of life.¹¹ Less than half of persons who die from advanced dementia access hospice care, due to lack of a predictable terminal phase of illness to match the 6-month prognosis criterion.^{26,27}

3.A.iv Hospitalization for acute illness is burdensome in advanced dementia. While as many as 67% of persons with advanced dementia ultimately die in a nursing home, hospitalization for acute illness is common in the final year of life.²⁸ In a national study of Medicare decedents with advanced cognitive impairment, 19% experienced at least one burdensome transition during the final 3 months of life.²⁹ One in ten nursing home residents with advanced dementia are admitted to intensive care in the final 30 days of life, and this practice is becoming more common over time.³⁰ In hospital, persons with dementia experience other treatments that may be more burdensome than beneficial, such as percutaneous feeding tubes, central lines, or physical restraints.^{31,32}

3.A.v Hospitalization for acute illness signals high risk of death in the coming months for persons with advanced dementia. Infections and nutritional decline typically precede death in advanced dementia.^{32,33,34} In CASCADE, the primary causes of hospitalization in advanced dementia were pneumonia, other infections, heart failure, hip fracture and dehydration.^{11,35} Six-month mortality risk for persons with advanced dementia who are hospitalized with pneumonia, septicemia, or hip fracture is 50%, and 20-40% for those who develop persistent feeding problems or dehydration.^{11,32,36,37} Thus, hospital admission for pneumonia, infection with septicemia, hip fracture, or

complications of feeding problems such as weight loss and dehydration are sentinel events identifying persons with advanced dementia and high risk of death in the next year.

3.A.vi Hospitalization for acute illness is a unique opportunity for patients with advanced dementia to access specialty palliative care. Current workforce projections make it unfeasible to propose a nursing home model of specialty palliative care for persons with advanced dementia. First, demand for palliative care greatly exceeds the specialty workforce, estimated to include fewer than 4000 physicians and 17,000 nurses.^{38,39} Second, geographic variation magnifies these workforce shortages -- Southeastern retirement in-migration states with large African-American populations lag other regions in palliative care.⁴⁰

Hospitalization may be burdensome, but it is also an opportunity to access specialty palliative care for this patient population. While only 27% of US nursing homes report any type of special services for palliative or end-of-life care, 63% of hospitals, and 85% of large hospitals have specialty palliative care services.^{41,42} Access to specialty palliative care is thus likely to remain rare in long-term care settings, but readily available in acute care hospitals.

3.A.vii Triggered consultation is effective to improve palliative care access in other diseases. The growing practice of triggered consultation has been shown to improve access to specialty palliative care for high need patient populations, including patients with advanced cancer or critical illness.^{43,44} First, attending physicians and specialty palliative care teams agree on clinical indicators of a need for palliative care consultation such as advanced stage incurable diagnoses and uncontrolled symptom distress. Next, patient electronic records are screened for these indicators. When a patient screens positive on the chosen indicators, the attending physician affirms the need and writes a consultation order. Triggers for palliative care consultation in advanced dementia, such as hip fracture, have been proposed but never tested.⁴⁵

3.A.viii The trajectory of dementia results in a prolonged phase of advanced stage illness and unique palliative care needs. The long trajectory of functional decline in dementia is unlike any other life-limiting illness.⁴⁶ In a thoughtful narrative review, Sachs summarized the unique aspects of dementia palliative care, all of which must be addressed in any palliative care intervention. First, dementia has a slow trajectory without a distinct terminal phase, making it difficult for clinicians and family caregivers to time transitions in goals of care. Second, symptom management is challenging due to loss of verbal communication for assessment, and concerns about medication side effects in frail patients. Third, the most common and important decisions involve treatments considered ordinary -- feeding options, antibiotics, or hospitalization.⁴⁷ The unique needs of this patient population demand a dementia-specific model of palliative care.

3.A.ix Specialty palliative care improves outcomes, but is unproven for advanced dementia.

High quality clinical trials and observational studies demonstrate the benefits of specialty palliative care for patients with advanced cancer and critical illness. Systematic access to palliative care teams results in improved treatment decision-making and quality of life for seriously ill patients and their families, while reducing costs.^{48,49,50,51,52} However, these studies do not generalize to the advanced dementia population, given the unique symptom management concerns and treatment decisions relevant to this disease.

No major clinical trial has tested a model of palliative care for advanced dementia. Only two small studies have been published. Ahronheim conducted a small randomized trial of geriatric palliative care consultation at a single hospital, enrolling n=99 patients with advanced stage dementia. The intervention resulted in increased use of palliative care plans (23% vs 4%, p=0.008) and a reduction in intravenous therapies (66% vs 81%, p=0.025), but had no effects on other invasive procedures, physical restraint use, or life-sustaining treatment decisions.⁵³ In a small pre-post study (n=52), Campbell tested proactive case-finding of patients with advanced dementia for palliative care in intensive care. Intervention patients experienced fewer hospital days (7.4 vs 12.1, p<0.007) and ICU days (3.5 vs 6.8, p<0.004), with no difference in mortality or overall treatment intensity.⁵⁴

3.A.x Conceptual Framework: Donebedian model applied to Palliative Care Domains. The design of this innovative approach to improve advanced dementia palliative care is grounded in the Donebedian model to analyze and explain the quality of healthcare, in order to measure the effects of health services innovations on patient-centered outcomes. This model is widely used to evaluate the quality of healthcare, and to design health services

research to test hypotheses about how changes in health care access and delivery will affect patient outcomes. The Donebedian model proposes causal relationships between the structural elements of healthcare (e.g. hospital staffing with specialty palliative care), care processes (e.g. palliative care consultations, family meetings to discuss goals of care) and desired patient outcomes (e.g. reduced 30-day hospital admissions, increased documentation of treatment preferences using POLST).^{55,56}

Since the overarching goal is to improve the quality of advanced dementia palliative care, the design of the intervention is mapped to the National Consensus Project (NCP) for Quality Palliative Care framework of guidelines and preferred practices.⁵⁷ Updated in 2013, the NCP defines best practices in 8 key palliative care domains: (1) structure and process (2) physical, (3) psychiatric, (4) social, (5) spiritual, religious, and existential (6) cultural, (7) care of the imminently dying patient, and (8) ethical and legal. The intervention design addresses the first domain (the structure and process of advanced dementia palliative care), by increasing access to specialty palliative care teams during hospitalization. Consultation content and resulting post-discharge care plans will address the remaining domains: physical symptoms, psychiatric symptoms, social support, spiritual support, cultural concerns, care of the imminently dying (when appropriate to prognosis), and ethical and legal dimensions of goals of care and treatment preference documentation.

SUMMARY OF SIGNIFICANCE AND INNOVATION

The proposed research is significant in seeking to ameliorate the extraordinary individual and public health impact of advanced dementia. Alzheimer's disease and other dementias affect millions of Americans and their family caregivers, extracting the highest family and societal costs of any leading cause of death. Prior research, much of it done by these investigators, demonstrates the extraordinary suffering caused by advanced dementia. Patients and families have extensive unmet palliative care needs, and current models of hospice and palliative care are poorly designed for advanced dementia. This pilot study, if successfully executed, matches a clear national research priority as demonstrated by the NIA Program Announcement (PA-13-354 Advancing the Science of Geriatric Palliative Care) and the National Alzheimer's Project Act.

The proposed research is innovative, as it will provide the first clinical trial of an advanced dementia palliative care model matched to the unique characteristics of this disease, in a novel setting, with components of collaborative care. Specialty palliative care has proven benefits for patients with advanced cancer; however, specialty palliative care has never been tested to improve outcomes for advanced dementia. Dementia's long trajectory of functional dependency, challenges in symptom assessment and management, and ethical demands for shared decision-making about "ordinary" treatments such as nutrition and antibiotics requires new approaches in palliative care consultation. The proposed intervention is innovative in moving research on dementia palliative care out of the nursing home -- where most research has focused -- and into the acute care hospital setting. Further, the approach is innovative as it explores the potential for collaborative palliative care, connecting hospital-based specialty palliative care clinicians with post-acute primary healthcare providers.

Study Aims

Alzheimer's disease and related dementias affect 5 million Americans at an annual cost of \$215 billion. Dementia is a contributing cause for 1 in 3 deaths, and is the only major cause of death with no effective prevention or treatment.

One million Americans have advanced dementia, characterized by inability to recognize family, sparse speech, and dependency for all activities of daily living. Median survival is 1.3 years, and 6-month mortality is 25%. Family care averages 22 unpaid hours per week for 3 years. Family expenses average \$66,000 in the last year of life – greater than any other cause of death.

The final year of life with dementia is characterized by hospitalizations for acute complications -- pneumonia and other infections, dehydration, malnutrition, falls and fractures. Acute illnesses cause symptom distress for patients, with emotional and financial strain for family caregivers. These illnesses are also associated with a high risk of death in the next year and raise ethical questions about goals of medical treatment.

Palliative care consultation improves outcomes for patients with advanced cancer and critical illness, but has never been rigorously tested for advanced dementia. Dementia-specific palliative care is needed to address the unique symptoms and treatment decisions relevant to this disease. Hospital admissions provide an opportunity to access specialty palliative care teams for patients with advanced dementia, at a time when acute illness signals worsening prognosis. Collaboration with primary providers is essential, since dementia's prolonged trajectory means most clinical care for dementia is provided at home and in nursing facilities.

We therefore propose to develop and pilot test a model of palliative care consultation for advanced dementia patients, triggered by hospitalization for a serious acute illness. After systematic refinement of operational protocols and tools with stakeholders, we will enroll persons with advanced dementia plus an acute illness associated with high risk of death in the coming year. Patients will be enrolled with their family decision-makers (N=60 dyads) in a randomized feasibility trial. Intervention dyads will receive specialty palliative care consultation during hospital admission, plus post-discharge collaborative care by their outpatient primary care provider and a palliative care nurse practitioner. Control dyads will receive usual care.

Our research objective is to generate preliminary data for a large multi-site randomized controlled trial (RCT) of a model of palliative care consultation for advanced dementia in an application to NIA (PA-13-354 *Advancing the Science of Geriatric Palliative Care*).

Our specific aims for this application are:

Aim 1: To develop a best-practice model of palliative care consultation for advanced dementia triggered by hospital admission for serious acute illness.

Aim 2: To conduct a pilot randomized trial of triggered palliative care consultation for advanced dementia (versus usual care) to demonstrate the feasibility of conducting a larger RCT and to estimate effect sizes to inform the larger RCT. The primary outcome will be **number of hospital transfers (emergency room or hospital admission) in the 30 days post discharge**. Secondary outcomes, measured at hospital discharge and 30 days follow-up, will include **number of palliative care domains in the care plan, hospice referral, POLST (Physician Orders for Life-Sustaining Treatment) form completion, decision not to re-hospitalize, and 60 day hospital transfers and burdensome treatments**.

H1: The dementia palliative care model will be feasible as demonstrated by full enrollment and 80% completion of intervention key components and outcomes data collection.

H2: Compared to usual care, intervention dyads will demonstrate trends in outcome measures -- fewer 30-day hospital transfers; increased number of palliative care domains in the care plan; increased hospice referral; increased POLST completion; increased decisions not to re-hospitalize and fewer burdensome treatments.

Methods

3.D.i Overview: The proposed 2-year study will develop a model for palliative care consultation for hospitalized patients with advanced dementia (Aim 1) and conduct a pilot study of an RCT to test the efficacy of this model (Aim 2). During the first 3 months investigators will work with an advisory group of stakeholders to refine intervention protocols. The study population will consist of N=60 dyads of persons with advanced dementia who are hospitalized with serious acute illness and their family decision-makers. Eligible patients will have baseline advanced dementia, corresponding to moderately severe to severe dementia using GDS staging of 5-7) and an acute illness associated with increased mortality risk (pneumonia, septicemia, hip fracture, malnutrition or dehydration complicating persistent feeding problems, or other similar condition). Each dyad will be randomized to specialty palliative care consultation followed by collaborative care with outpatient primary providers vs. usual care. The dyad will be the unit of analysis. The primary outcome will be **number of hospital transfers in the 30 days post-discharge, defined as visits to an emergency department or acute care hospitalization**. Secondary outcomes, measured at hospital discharge and 30 days, will include **number of palliative care domains in the care plan, hospice referral, POLST (Physician Orders for Life-Sustaining Treatment) form completion, decision not to re-hospitalize, 60-day hospital transfers and burdensome treatments**.

3.D.ii Methods to meet Aim 1: To develop a best-practice model of palliative care consultation for advanced dementia triggered by hospital admission for serious acute illness.

During Year 1 (months 1-3) investigators will complete developmental steps to refine the model of palliative care consultation for advanced dementia with input from key stakeholders who address practical aspects of implementation. Investigators will convene a Stakeholder Advisory Group (SAG) composed of hospital-based attending physicians from services that commonly take care of advanced dementia patients (N=3), nursing home or community based primary physicians, nurse practitioners or physician assistants (N=3), and family caregivers for persons with advanced dementia (N=3). Stakeholders will be asked to meet 3 times to provide recommendations on 1) identification of eligible patients for advanced dementia palliative care consultation, 2) meaningful use of educational tools for family caregivers, and 3) collaborative care in transitions from hospital to primary care settings.

Step 1: Identification of eligible patients for advanced dementia palliative care consultation. Investigators will develop a method to screen hospital admissions for rapid identification of eligible patients. This will require electronic screening for dementia diagnosis plus selected serious illness diagnoses, followed by confirmation of dementia stage using descriptions of baseline function based on the GDS. Investigators will review the most recent 12 months of data from the UNC Hospital discharge database for service location of patients admitted with paired diagnoses of dementia plus one of the serious acute illnesses -- pneumonia, septicemia, hip fracture, or complications of feeding problems such as dehydration, protein malnutrition or failure to thrive. In 2014, 567 patients were discharged with dementia plus one of these acute illnesses, indicative of adequate population for this screening approach.

Attending physicians for services with high admission rates for these patients will be asked to approve daily census screening in the electronic health record for these paired diagnoses, and for evidence suggestive of advanced dementia stage. Admission census screens will be completed by a Palliative Care Nurse Practitioner, who will then contact the attending physician for permission to approach the patient's family caregiver about the study. Family caregivers will be asked to confirm dementia stage using functional descriptions of GDS 5, 6 or 7, and to give consent for study participation. The attending physician will also authorize consultation should the patient-family dyad enroll and be randomized to intervention. The SAG will assist investigators to ensure this approach fits hospital physician practice and meets patient and family caregiver needs.

Addressing a potential threat to validity: Consultation can be ineffective if implemented without attention to patients' right to refuse services and respect for the professionalism of the attending physician. From our experience with triggered consultations, currently used at UNC Hospital for patients with Stage IV gynecologic cancers and with advanced systolic heart failure, the UNC Palliative Care physicians and nurse practitioners have developed an effective approach to gain entrée with referring teams, patients and family caregivers. Attending physicians will be

permitted to refuse triggered consultations, as will patients and families; acceptance of consultation will allow billing for professional time but not for other research activities.

Table 1: Evidence-based Educational Tools

Tool	Content	Planned Use
BOOKLET <i>Advanced Dementia: A Guide for Families</i>	1) What is Advanced Dementia 2) Determining the Primary Goal of Care 3) Approach to Decision-making 4) Approach to Eating problems 5) Decisions about Hospitalization 6) Treatment decisions for infections 7) How Advanced Dementia affects Family 8) Hospice and Palliative Care	UNIVERSAL USE: Booklet will be given to and reviewed with all intervention family decision-makers.
NURSE-GUIDED FAMILY EDUCATION <i>IN-PEACE Caregiver Manual</i>	Over 20 print educational summaries on key topics for family caregivers; examples include: <ul style="list-style-type: none"> • Caregiver stress • Communicating with the person with dementia • Bathing techniques • Feeding techniques • Responding to pain • Responding to sundowning • Dental care • Help with sleeping • Depression in dementia 	SELECTIVE USE: Consultants will select and provide materials targeted to the needs of each family caregiver.
DECISION AID <i>Making Choices: Feeding Options for Patients with Dementia</i>	Video decision aid defining the pros and cons of the treatment choice between tube feeding and assisted feeding in advanced dementia.	SELECTIVE USE: Consultants will view the decision aid with family caregivers when treatment options for eating problems are being considered.

Step 2: Meaningful use of educational tools for advanced dementia family caregivers. Drs. Hanson, Mitchell and Sachs have developed evidence-based tools to educate family decision-makers and support meaningful shared decision-making related to advanced dementia. (Table 1) These tools include the educational booklet developed by Dr. Mitchell and used the pilot test of hospital consultation (3.C.vi); a video decision aid developed by Drs. Hanson and Mitchell for the decision between assisted feeding and tube feeding (3.C.iv); and dementia care protocols used by nurse practitioners to support family caregivers developed by Dr. Sachs for the PEACE study (3.C.v). The SAG will review tools and discuss ways to make them meaningful for families.

Step 3: Collaborative care in transitions from hospital to primary care settings. Care transitions are critical junctures for all patients; however most transitional care studies have excluded dementia patients. To be effective, hospital-based palliative care teams must collaborate with primary providers since most dementia care is provided in long-term care and community settings.⁵⁸ Therefore, at the time of hospital discharge, the specialty Palliative Care team will complete a structured care plan addressing domains of palliative care. When supported by communication with the family decision-maker, they will also complete and sign a Medical Orders for Scope of Treatment (MOST) form. MOST is the North Carolina version of the POLST paradigm, a multi-state portable order set proven effective to enhance treatment consistent with patient preferences across healthcare transitions.^{59,60} The Palliative Care Plan and the MOST will be provided in print and fax format to the patient's primary provider, followed by a post-discharge telephone call from the Palliative Care Nurse Practitioner to ensure receipt and answer questions. Working with the SAG, investigators will develop a practical and flexible procedure for collaborative

care to ensure effective hand-off to the primary provider and ways to address post-discharge palliative care concerns.

3.D.iii Methods to meet Aim 2: To conduct a pilot randomized trial of triggered palliative care consultation for advanced dementia (versus usual care) to demonstrate the feasibility of conducting such a trial and to generate data to estimate effect sizes to inform a larger RCT.

During Year 1 (months 4-12) through Year 2 investigators will conduct the pilot RCT and measure outcomes using hospital chart review at discharge and family decision-maker interviews at enrollment and 30 and 60 days post hospital discharge. Specific aspects of the pilot RCT will be informed by results from Aim 1.

3.D.iv Study Site: All study participants will be recruited at the University of North Carolina Hospital during admission for acute illnesses. UNC Hospital is a public academic healthcare complex of 5 hospitals -- Medical-Surgical, Women's Health, Neurosciences, Cancer, and Pediatrics -- with 783 licensed beds serving over 37,000 admitted patients annually. Faculty physicians appointed in the UNC School of Medicine provide all medical services.

3.D.v Study Participants and Recruitment: Study participants will be n=60 dyads of patients with GDS Stage 5-7 dementia from any underlying cause who are hospitalized with a serious acute illness and their family decision-maker. Inclusion Criteria: The Palliative Care Nurse Practitioner (PCNP) and Project Manager will screen target inpatient census lists every day for patients with a diagnosis of dementia and a qualifying acute illness, under a HIPAA waiver. The PCNP or Palliative Care physician will contact the attending physician to confirm the qualifying diagnoses and probable stage of dementia, as well as to obtain permission to approach the family decision-maker about study participation, including consultation if randomized to intervention. Patients will be eligible if they are aged 65 or older and have a physician-confirmed a) diagnosis of dementia, b) advanced dementia scored as 5, 6 or 7 on the Global Deterioration Scale (GDS), and c) hospital admission for pneumonia, septicemia, hip fracture, protein malnutrition, dehydration or similarly serious acute illness. Dementia stage will be confirmed for eligibility with family decision-makers by showing them the GDS Stage descriptions and asking them to select the description most consistent with the patient's pre-admission functioning. If family decision-makers are uncertain, the Palliative Care Nurse Practitioner will request permission to contact the primary provider for this information.

Eligible family decision-makers will be defined as the family caregiver with the greatest involvement in decision-making. If two family caregivers share this role the legally authorized representative will be eligible, but may include input from others.⁶¹ Exclusion Criteria: Patients will be excluded if they do not have a family surrogate decision-maker. Family decision-makers will not be eligible if they cannot complete interviews in English, or if the treating physician believes participation would cause undue stress.

Addressing a potential threat to validity: During the pilot study by Mitchell (3.C.vi) barriers to identification of eligible patients and to consultation were discovered. In addition, during the development phase of this trial, precise staging was confounded by acute illness symptoms. These barriers are addressed in this design by using more sensitive screening criteria, broadening eligibility to GDS stages 5, 6 and 7, and use of clinician-to-clinician communication to affirm consultation orders.

3.D.vi Human Subjects: Once an eligible patient-family decision-maker dyad is identified and attending physician approval is obtained, the Project Manager / Data Collector will obtain informed consent from the family decision-maker; consent will be obtained prior to randomization. All study procedures will be subject to IRB review at the University of North Carolina, which will serve as the sole study site. Study risks include emotional distress and confidentiality; protections will include strict training of study staff, data security, and strategies to address family emotional distress with compassion, flexibility and appropriate referrals to supportive resources. Treatment plans will be controlled throughout the study by attending physicians providing direct care to patients who are enrolled, regardless of group assignment.

3.D.vii Training for Intervention Protocols: In Year 1, investigators developed a templated, structured approach to intervention protocols to ensure consistent delivery of the intervention. All Palliative Care consultation will

initially be provided by a small group of 3 members of the Palliative Care specialty team to promote consistent quality -- Kyle Terrell, NP, Laura Hanson, MD and Chrissy Kistler MD -- who are trained in the intervention protocol. Their training includes knowledge of clinical evidence for advanced dementia palliative care, educational tools and their use in consultations, completion of advanced dementia Palliative Care Plans, MOST form completion, and principles of shared decision-making and the VALUE (Value family comments, Address family concerns, Listen, Understand the patient as a person, Elicit family questions) framework to guide family meetings and discussion of goals of care.^{62, 63, 64, 65} Physicians and nurse practitioners will gain access to an electronic health record template for consultation. Dr. Hanson will provide this training, and be available for follow-up questions as consultations are completed.

3.D.viii Randomization: The dyad will be the unit of randomization and analysis. Decision-makers who provide informed consent for participation will then be randomized by the study statistician in a 1:1 ratio to intervention vs. control. Allocation will be revealed to the specialty Palliative Care team, but will be concealed from the Project Manager / Data Collector who will collect outcome measures during follow-up interviews.

3.D. ix Intervention Condition: Patient-family dyads randomized to the intervention group will receive specialty inter-disciplinary Palliative Care consultation during hospitalization with post-discharge collaborative care by a Palliative Care Nurse Practitioner and outpatient primary care physician. The consultation will consist of at least one visit with the patient and their family decision-maker, with additional visits consistent with clinical needs. Consultation will address a) prognosis and trajectory of advanced stage dementia, b) assessment and treatment of pain and other physical symptoms, c) assessment and management of neuropsychiatric symptoms, c) social support including caregiver stressors, d) spiritual support needs for patient or caregivers, e) cultural concerns framing care, and f) goals of care and g) key clinical decisions such as feeding options, antibiotic use, invasive procedures, or re-hospitalization. All intervention families will receive and review a copy of the booklet on Advanced Dementia (Table 1). Access to other evidence-based educational and decision aid tools for family decision-makers will be selective, based on needs discovered during consultation.

For the collaborative care component of the intervention, the Palliative Care physician or nurse practitioner will prepare a Palliative Care plan in printed form, as well as a copy of the MOST form if discussed and signed during consultation. Copies of the Palliative Care Plan and the MOST form will be given to the primary family decision-maker prior to discharge. These documents will be mailed and faxed to the patient's primary provider. The Palliative Care Nurse Practitioner will then make follow-up calls to the family decision-maker and the primary provider within 72 hours and again contact the family caregiver within 2 weeks after discharge to discuss concerns or questions related to the Palliative Care plan, and to facilitate access to post-acute services if needed. Calls to family caregivers will follow a semi-structured script [see attached], but calls to primary providers will not, and will be modified to e-mail or electronic health record communication at the preference of the provider. Up to 3 call attempts will be made for each contact.

3.D.x Control Condition: Patient-family decision-maker dyads randomized to the control group will receive usual hospital and post-acute care. To encourage participation, they will also be offered a copy of the Alzheimer's Association free booklet *Tips for Late-Stage Caregivers*, which addresses common problems but does not duplicate any of the intervention tools.

Addressing a potential threat to validity: Palliative care services cannot be ethically withheld from patients in the control group. Palliative care consultation will be permitted for controls, but these consultations will not use intervention protocols and tools, and will not include post-discharge collaboration with primary providers. Training to palliative care clinicians may dilute the measurement of differences between groups. However, advanced dementia is currently rare as a palliative consultation diagnosis at UNC Hospitals, accounting for only 20 of 685 patients in 2013.

3.D.xi Baseline and Follow-up Data Collection: Data collection will be identical for intervention and control groups. Study measures will be obtained from **Hospital Chart Reviews** covering the enrollment admission AND from family decision-maker interviews at enrollment (**Family Baseline Interview**) and at 30 days post-discharge (**Family Follow-up Interview**) 60 days post-discharge (**60 Day Family Follow-Up Interview**). Family decision-

makers will be offered flexibility in timing of interviews. Our team has extensive experience with after death interviews; an After-Death version of the 30 and 60-day Interview will be designed to be sensitive to bereaved family.

3.D.xii Measures for Feasibility and Fidelity to the Intervention (Aim 2, Hypothesis 1)

H1: The dementia palliative care model will be feasible as demonstrated by full enrollment and 80% completion of intervention key components and outcomes data collection.

Measures of feasibility will include enrollment and data completion rates (intervention and control) and fidelity to key components of the advanced dementia palliative care consultation (intervention). Measures will be obtained from research enrollment tracking forms, hospital chart reviews, and call sheets kept by the Palliative Care Nurse Practitioner for communication post-discharge. Investigators will track enrollment and data completion rates, with targets of full enrollment and 80% data completion. For fidelity, investigators will measure completion of 5 key components of the intervention: initial consultation, transmission of Palliative Care Plan to family, transmission of Palliative Care Plan to primary care provider, completion of 2 follow-up calls to family decision-maker, and completion of 1 follow-up call to primary provider. Fidelity to the intervention will be met when there is completion of 4 of 5 (80%) key components.

3.D.xiii Outcome Measures for the Intervention (Aim2, Hypothesis 2):

H2: Compared to usual care, intervention dyads will demonstrate trends in outcome measures -- reduced hospital transfers; increased number of palliative care domains in the care plan; increased hospice referral; increased POLST completion; increased decisions not to re-hospitalize and fewer burdensome treatments.

Analyses to examine effects of the intervention vs. usual care will focus on outcomes with the greatest impact on patient and family experience during and up to 60 days after hospitalization. (Table 2)

Table 2: Aim 2 Primary and Secondary Outcomes and Sources of Data

Outcome	Measure	Source
<i>PRIMARY OUTCOME Aim 2:</i> 30-day hospital transfers	Number of hospital transfers (ED visits + hospital admissions) within 30 days after discharge.	Family Follow-up Interview
<i>SECONDARY OUTCOME Aim 2:</i> <i>Patient Comfort</i>	Comfort at the End of Life in Dementia (C-EOLD)	Family Follow-up Interview
<i>SECONDARY OUTCOME Aim 2:</i> <i>Family Distress</i>	Family Distress in Advanced Dementia Scale	Family Follow-up Interview
<i>SECONDARY OUTCOME Aim 2:</i> 30-day referral to hospice or palliative care post-discharge	% of patients with referral to hospice or outpatient palliative care from discharge to 60 days follow-up	Hospital Chart Review Family Follow-up Interview
<i>SECONDARY OUTCOME Aim 2:</i> POLST (MOST) completed	% of patients with MOST form completed	Hospital Chart Review Family Follow-up Interview
<i>SECONDARY OUTCOME Aim 2:</i> Palliative Care Domain Index	Number of palliative care domains addressed in the plan of care at hospital discharge (range 0-10)	Hospital Chart Review
<i>SECONDARY OUTCOME Aim 2:</i> Decision not to re-hospitalize	% of patients with do-not-hospitalize decisions	Hospital Chart Review Family Follow-up Interview
<i>SECONDARY OUTCOME Aim 2:</i> Use of burdensome treatments	Total number of the following treatments used: feeding tube, central intravenous line, surgical procedure, ICU transfer, ventilator use, CPR use	Hospital Chart Review Family Follow-up Interview
<i>SECONDARY OUTCOME Aim 2:</i> 60-day hospital transfers	Number of hospital transfers (ED visits + hospital admissions) within 60 days after discharge.	Family Follow-up Interview

- **PRIMARY OUTCOME-- 30-day hospital transfers** will be measured during Family Follow-up Interviews by asking how many times the patient with advanced dementia has been to an emergency room and how many times

he / she has been admitted to a hospital within the time frame of interest; chart review is not feasible for this data as patients come from a wide geographic area with many hospitals.

- **SECONDARY OUTCOME -- Patient Comfort** will be measured in Enrollment and Family Follow-up Interviews, using the reliable and valid Comfort at the End of Life in Dementia (C-EOLD) which includes 1 week recall of patient comfort with multiple symptom items; 10 items are rated 1-4 and summed, for a range of 10-40. It has good internal consistency (Cronbach's alpha 0.83-0.90) and convergent validity ($r=0.81$ with the Decision Satisfaction Inventory).^{66,67}
- **SECONDARY OUTCOME --Family Distress** will be measured in Enrollment and Family Follow-up Interviews, using the Family Distress in Advanced Dementia
- **SECONDARY OUTCOME -- 30-day referral to hospice or outpatient palliative care** will be measured using Hospital Chart Review for referrals at discharge AND Family Follow-up Interviews for data on subsequent referrals.
- **SECONDARY OUTCOME -- POLST (MOST) completion** will be measured in Hospital Chart Review by tracking the presence or absence of a completed POLST paradigm form (MOST) in the discharge packet; to detect new POLST form completion post-discharge we will ask this as a single item in the Family Follow-up Interview.
- **SECONDARY OUTCOME -- Palliative Care Domain Index** is a Hospital Chart Review count of the presence or absence of information addressing 10 domains of palliative care in a patient's treatment plan -- prognosis, overall goals of care, physical symptoms, psychiatric symptoms, spiritual needs, and 5 treatment preferences: resuscitation, artificial feeding, intravenous fluids, antibiotics, and hospitalization. Each domain is scored as present or absent for a range of 0-10. Domains are scored based on whether or not they are addressed, not on choices for or against specific treatments. This measure is developed and currently in use for Dr. Hanson's Goals of Care clinical trial (3.C.iii) and has good inter-rater reliability ($\kappa=0.90$).
- **SECONDARY OUTCOME -- Decision not to re-hospitalize** will be measured in Hospital Chart Review as the percent of patients with a decision against re-hospitalization documented at the time of discharge; to detect new decisions post-discharge we will ask this as a single item in the Family 30-day Interview and 60-day Interviews.
- **SECONDARY OUTCOME -- Burdensome treatments** will be measured in Hospital Chart Review for the enrollment admission AND Family 60-day Interviews for the post-discharge period to generate a count per patient of use of the following treatments: feeding tube, central intravenous line, surgical procedure, ICU transfer, ventilator use, CPR use at any time during the time frame of interest.
- **SECONDARY OUTCOME-- 60-day hospital transfers** will be measured during Family Follow-up Interviews by asking how many times the patient with advanced dementia has been to an emergency room and how many times he / she has been admitted to a hospital within the time frame of interest; chart review is not feasible for this data as patients come from a wide geographic area with many hospitals.
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3.D.xiv Measures of Covariates

- **Patient demographics** – age, gender, race and ethnicity, religious affiliation (Family Enrollment Interview)
- **Family Decision-maker Demographics** – age, gender, race and ethnicity, religious affiliation, relationship to patient (Family Enrollment Interview)
- **Pre-admission residence** -- as private home, assisted living facility, nursing home or other (Hospital Chart Review)
- **Major co-morbid diagnoses** -- (Hospital Chart Review)
- **Functional status** – measured using the Bedford Alzheimer Nursing Severity scale for function in advanced dementia; this scale ranges from 0-28 with higher scores indicating worse function ($\alpha=0.80$, Pearson's $r=0.62-0.79$)⁶⁸ (Family Enrollment Interview)
- **Dementia stage** – measured using the valid and reliable Global Deterioration Scale (GDS) (Family Enrollment Interview AND Family Follow-up Interview)
- **Advance directives** – measured by recording presence or absence of a living will or Health Care Power of Attorney (Family Enrollment Interview)

- **Discharge location** -- measured as private home, assisted living facility, nursing home or other (Hospital Chart Review)
- **Survival** will be measured for each patient as days from study enrollment to death up to and including 60 days follow-up (Hospital Chart Review and Family Follow-up Interview)
- **Family Decision-maker knowledge of advanced dementia** will be measured using an 18-item true / false Knowledge Index with content on advanced dementia, treatment options and their outcomes. These items have been previously developed by Dr. Hanson and used in prior studies. (Family Enrollment)
- **Family Decision-maker perception of prognosis** will be measured using a single item asking what they expect will happen to the patient during the next 6 months, with response options of “get better,” “stay about the same,” “get worse” or “likely to die.” (Family Enrollment, 30-day Interview, and 60-day Interview)

3.D.xv Analysis

Analyses to meet **Aim 2, Hypothesis 1** will be purely descriptive. We will calculate and report the percent of eligible dyads approached who enrolled, and the percent who were retained to study completion with data collection on outcome measures. We will describe fidelity to the 5 key components of the intervention. We will summarize any barriers to study enrollment and retention, or fidelity, in order to enhance protocols for a future clinical trial.

Analyses to meet **Aim 2, Hypothesis 2** will begin by examining the validity of randomization by comparing intervention and control participants on baseline measures. Any variables that are not equally distributed between groups could potentially bias results. An adjusted analysis that includes these variables as covariates will be implemented.

Descriptive analyses of all major variables will be carried out to examine their distributions, influential data points, and missing data. If the amount of missing data on any individual independent variable is small and the pattern of missing data both within and among variables is reasonably random, we will exclude subjects in analyses with missing data. However, we will use the method of multiple imputation for sensitivity analysis to ensure the robustness of the analysis results.⁶⁹ Categorical variables will be collapsed into meaningful groups. Continuous variables that are poorly distributed may be transformed, categorized or analyzed using non-parametric tests. Two-sample t-tests or Fisher exact tests will be used when appropriate for the comparison between intervention and control groups, with adjustments for multiple comparisons. Generalized estimating equations (GEE) with an exchangeable dependence structure will be used to test the overall intervention effect. All statistical tests will be 2-tailed with an overall 0.05 significance level for pre-specified analyses. The secondary outcomes will be analyzed similarly and alphas will also be adjusted for multiple comparisons.⁷⁰

For a dichotomous primary outcome (hospital transfer), the sample size of 60 patients with 30 patients per group gives 81% power to detect a relative risk of 2.7, assuming that 25% of the patients in the control group would have a positive/presence outcome. The power is calculated based on Fisher’s exact tests with a significance level $\alpha=0.05/2=0.025$. For a normally distributed continuous outcome (Palliative Care Domain Index), our current sample size gives 79% power to detect an effect size of 0.8 in Cohen’s *d* based on a 2-sample t-test with equal variation in two groups. The effect size is large according to general guidelines using Cohen’s *d*. We anticipate collecting sufficient data to determine the true effect size for future clinical trials.

Research Ethics

Data Management and Storage

The study database complies with current data security standards, and provides real-time data entry validation, and provides audit trails documenting any changes or corrections of the study data. Data entry or review requires logging into a secure portal with a username and password. The database is hosted by the Cecil Sheps Center for Health Services Research at the University of North Carolina-Chapel Hill, and is HIPAA-compliant. Explicit

identifying information will be recorded on separate forms and will NOT be sent to the database; these forms will be maintained in a secure location.

Human Subjects

Protection of Human Subjects

Participants and Eligibility: The target population is n = 60 persons with advanced dementia paired with n=60 family decision-makers (30 dyads in control, 30 in intervention group). Persons with dementia are participants, but family surrogate consent and participation is required for all of them, as the severity of their dementia will make them incapable of informed consent. If two family caregivers share this role the legally authorized representative will be eligible for study enrollment. Surrogate decision-makers identified for each eligible nursing home resident are defined as a) their guardian, b) Health Care Power of Attorney, or if no HCPOA is available, c) the usual family surrogate decision-maker identified by the primary physician.

Enrollment and Informed Consent: The Palliative Care Nurse Practitioner or Project Manager will screen target inpatient census lists every day for patients with a diagnosis of dementia and a qualifying acute illness, under a HIPAA waiver. She will contact the attending physician to confirm the qualifying diagnoses and probable stage of dementia, as well as to obtain permission to approach the family decision-maker about study participation, including sharing basic information about the study. The Project Manager will speak with the surrogate decision-maker in a private area to discuss the study and obtain informed consent. Once enrolled, study participants in both the control and intervention groups will be followed up to 2 months. Due to change in funding, Investigators decided to add an additional follow-up interview (60-day interview). The Project Manager will attempt to re-consent all participants to date all to allow for a 60-day follow-up call. The Project Manager will do this by mailing participants an addendum consent, and have them return a response card. The card will indicate “yes, please contact me” or “no, please do not contact me”. For all participants who send the card back saying “yes”, we’ll re-consent. For everyone who mails it back saying no, we will not contact them. For all those who don’t mail any card back, we will call them to see if they are interested in the additional 60-day interview.

Potential Risks: The primary risk of this study for family surrogates is *emotional distress* related to learning more about dementia prognosis and goals of care decisions for a frail and cognitively impaired family member. Participation in the study, particularly in the intervention group, may draw family members’ attention to serious illness, and may result in anxiety or sadness over the health consequences of these problems.

A potential risk is *breach of confidentiality*, given that investigators will collect personal health information about the person with advanced dementia.

Adequacy of Protection Against Risks: All study procedures, informed consent forms, and recruitment procedures will undergo review by the Institutional Review Board at the University of North Carolina-Chapel Hill prior to initiating research, and will be subject to annual and other required reviews.

All family decision-makers will provide written informed consent for their participation, and surrogate informed consent for the participation of the person with advanced dementia for chart review data collection. Through the informed consent process, we will address the risks of *emotional distress* for family surrogates, or *breach of confidentiality* for the person with dementia.

To address the risks of *emotional distress*: Investigators will include attention to emotional distress during training on the intervention protocol for Palliative Care team members, and for the Project Manager / Data Collector. Subjects will be informed that they do not have to respond to questions if they feel uncomfortable and they may stop the interview at any time. Distressed surrogates will be provided with a referral source including on-site social workers at each facility for emotional distress and hospice for bereavement support. The likelihood the family subject may need a referral source for dealing with emotional distress will be less than 1%.

To address the protection of *confidential medical information*: All health status and health care utilization data will be recorded without personal identifiers. Data will be entered in a password protected secure database, and all documentation will be maintained in locked files. All identifying information will be destroyed once all analysis and reporting is complete. At no time will personal identifying information be stored with the interviews, and no

identifying information will be stored on portable laptop computer devices used in field interviews. Participants will not be identified in any report or publication about this study. The procedures to minimize risks will help ensure a breach of confidentiality is rare occurring less than 1%.

Potential Benefits of the Proposed Research to Subjects and Society: Study participants may benefit from the palliative care consultation in the intervention group. All participants may benefit from the increased opportunity to communicate about the experience of family caregiving for advanced dementia. Societal benefits include enhanced understanding of interventions to improve the quality of palliative care for advanced dementia. If this trial has positive effects, the methodology has broad potential application and will be proposed for testing in a larger, and more definitive, randomized controlled trial design.

Data Safety Monitoring

This study poses minimal risks. Any unanticipated problems or adverse events will be reported to the PI immediately. The study does not have any stopping rules. The PI will review and unanticipated problems or adverse events and decide of subject withdrawal is in the best interest of the subject. A Data Safety Monitor, Dr. Cathleen Colon-Emeric, will meet every 6 months during data collection and data analysis with Dr. Hanson, Dr. Lin and Project Manager Stacey Gabriel. Dr. Colon-Emeric will review study protocols and preliminary data to ensure safe procedures are followed for this relatively vulnerable population.

Dissemination Plan

Dr. Hanson will present and discuss results from this pilot randomized controlled trial at the Kathleen Foley Palliative Care Retreat & Research Symposium. The research team will work together to submit pilot trial methods and results to a national peer-reviewed clinical journal in at least one publication.

Study results will be used to demonstrate the feasibility of a palliative care consult intervention tailored to meet the needs of patients and families facing advanced dementia. Our research analyses will provide preliminary evidence for the potential of this intervention to improve outcomes for patients with advanced dementia and their families. Investigators will use data from Aim 2 to establish the potential effect sizes of this intervention on important clinical outcomes, and to estimate the necessary sample size for a definitive efficacy clinical trial of this intervention. Given the long trajectory of even the most advanced stages of dementia care, we anticipate extending the collaborative care component in a larger efficacy trial.

During Year 2, this investigative team will submit a grant application for a multi-site randomized controlled trial (RCT) of a model of triggered palliative care consultation with enhanced collaborative care for advanced dementia, in an application to NIA (PA-13-354 *Advancing the Science of Geriatric Palliative Care*).

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